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09/269,903	05/06/1999	PETER JAMES WATTS	WC131	1775

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EXAMINER	
CHOI, FRANK I	

ART UNIT	PAPER NUMBER
1616	33

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/269,903	Applicant(s) WATTS, PETER JAMES	
	Examiner Frank I Choi	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/17/03,7/30/03* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *30* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29-57 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compositions comprising pellets and the specified drugs having a free acid group, a pKa in the range of 2.0-9.0, and is an alkali metal salt that has a higher solubility at pH 4.5-8 than a free acid form of the drug, where the means of releasing the drug in the terminal ileum or colon is by the use of the disclosed coating compounds having an appropriate pH dissolving range does not reasonably provide enablement for means not specifically disclosed or drugs in general, including drugs only described by their intended use. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The invention is directed to compositions and methods wherein a drug having a free acid group, a pKa in the range of 2-9, is present in the composition as an alkali metal salt that has a higher solubility at pH 4.5 to 8.0 than a free acid form the drug is contained in the inner core of a pellet coated with a rate controlling membrane and composition is prepared or formulated to prevent release of the drug until the composition reaches the terminal ileum or colon.

(2) The state of the prior art

The prior art of record appears to use the same materials but do not appear to disclose means other than what is specifically described by Applicant for preventing release of the drug until the composition reaches the terminal ileum or colon. Other than what Applicant has disclosed in the Specification, the prior art of record does not appear to disclose drugs having a free acid group, a pKa in the range of 2-9, in which the alkali metal salt has a higher solubility at ph 4.5 to 8.0 than a free acid form of the drugs.

(3) The relative skill of those in the art

The relative skill of the those in the art is high with respect to the specifically disclosed compounds having the appropriate pH range which are used as means of preventing release of the drug until the composition reaches the terminal ileum or colon. However, the relative skill of those in the art as to means which are not specifically disclosed appears to be low (See Hardy et al., Drug Delivery to the Gastrointestinal Tract, pgs. 87,88 (dissolving pH of the enteric polymer is critical, too low and the drug is released in the stomach, too high and insufficient drug is

released in the small intestine; for example, shellac, which Applicant has described as being suitable, due to its high pH solubility failed to provide sufficient drug absorption). Because of the state of the art above, it appears that the relative skill of those in the art is low relative to drugs having a free acid group, a pKa in the range of 2-9, in which the alkali metal salt has a higher solubility at ph 4.5 to 8.0 than a free acid form the drugs.

(4) The predictability or unpredictability of the art

The unpredictability of the art for a means of releasing the drug until the composition reaches the terminal ileum or colon is high. According to Hardy et al., the "current, widely accepted compendial test criteria are poorly predictive of release in man". Id. at pg. 94. Further, the reliability and predictability of targeting delivery in therapeutically effective amounts is dependent on selection of the coating polymer. Id. In light of (2) and (3) it appears that the predictability of the art relative to drugs which having a free acid group, a pKa in the range of 2-9, in which the alkali metal salt has a higher solubility at ph 4.5 to 8.0 than a free acid form the drugs is low.

(5) The breadth of the claims

The claims are very broad. The claims either do not mention what the means of preventing release in terminal ileum or colon are or broadly mention a membrane, or enteric coating or specific polymer but do not mention the pH dissolve range which appears to be critical. Further the claims, except where specific drugs are mentioned, describe the drugs by intended use or function.

(6) The amount of direction or guidance presented

The only drugs specifically described are ridogrel, thromboxane synthase A2 inhibitors thromboxan A2/prostaglandin endoperoxide receptor antagonsists disclosed which the Specification indicates are disclosed in US 4,963,573 and sodium cromoglycate. Further, the specification does not appear the indicate what drugs would be suitable for treatment of ulcerative colitis, Crohn's disease, irritable bowel syndrome or inflammatory bowel disease or the appropriate dose of these undisclosed drugs. Other the specifically described polymers and pH values, the specification does not appear to disclose what other means would be suitable for preventing release of the drug until the composition reaches the terminal ilium or colon. See In re Dreshfield, 45 USPQ 36 (CCPA 1940) ("It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result." A disclosure should contain representative examples which provide reasonable assurance to one skilled in the art that the compounds fall within the scope of a claim will possess the alleged activity. See In re Riat et al. (CCPA 1964) 140 USPQ 471; In re Barr et al. (CCPA 1971) 151 USPQ 724.

(7) The presence or absence of working examples

As stated above, the specification provides limited examples of specified drugs and means of preventing release of the drug until the composition reaches the terminal ileum or colon.

(8) The quantity of experimentation necessary

In light of the above, it appears that one of ordinary skill in the art would be required to do undue experimentation in order to determine suitable drugs, appropriate dosages for administration in the terminal ileum or colon and other means for preventing release of the drug until the terminal ileum or colon is reached.

Examiner has duly considered Applicant's arguments but deems them unpersuasive.

Examiner agrees with Applicant that formulating a compound to effect rate of release would not involve undue experimentation, but the same is not true where selected delivery into the terminal ileum or colon is desired. Applicant cites Hardy et al. as evidence that additonal meands are well known in the art. However, as indicated above, Hardy et al. supports the position that one of ordinary skill in the art would be required to do undue experimentation to determine means other than the use of the specified polymers which additionally have suitable pH dissolving ranges. Applicant's argument that undue experimentation would not be necessary does not appear to be supported by sufficient probative evidence. In any case, the rejection is based on scope of enablement, i.e., the enablement provided by Applicant is no sufficient to enable the entire scope of Applicant's claims.

Examiner has duly considered Applicant's arguments but deems them unpersuasive.

Applicant arguments do not appear to be supported by evidence. Examiner has provided evidence on the issue of enablement. Applicant's arguments that the reference predates the filing of the present invention do not overcome the rejection herein. The arguments of counsel do not constitute evidence sufficient to overcome the rejection. See In re Knowlton, 183 USPQ 33, 37 (CCPA 1974); In re Wiseman, 201 USPQ 658 (CCPA 1979). Applicant argues that it has disclosed in the specification suitable drugs and has provided examples and that means for colon

delivery were well known in the art. However, the reference provided was authored by the inventor and does not appear described any more than what is described in the Specification. The written description requirement is separate and distinct from the enablement requirement. In re Barker, 559 F.2d 588, 194 USPQ 470 (CCPA 1977), cert. denied, 434 U.S. 1064 (1978); Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991) (While acknowledging that some of its cases concerning the written description requirement and the enablement requirement are confusing, the Federal Circuit reaffirmed that under 35 U.S.C. 112, first paragraph, the written description requirement is separate and distinct from the enablement requirement and gave an example thereof.). See In re Armbruster, 512 F.2d 676, 677, 185 USPQ 152, 153 (CCPA 1975) ("[A] specification which describes' does not necessarily also enable' one skilled in the art to make or use the claimed invention."). Finally, Applicant's arguments concerning In re Dreshfield do not overcome the rejection. Applicant is directed to Wands Factor (6) above, where the argument did not simply concern drugs but also the means of delivery.

Claims 29-57 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting one or more of the following essential elements or steps, such omission amounting to a gap between the elements or steps. See MPEP § 2172.01. The omitted elements or steps are: the specified polymer and pH dissolve range of said polymer which is used to coat the composition and prevent release of the drug until the composition reaches the terminal ileum or colon. Applicant argues that pH is implicit in the claims, however, Applicant argues that polymer and pH are not critical to the invention. If so, Applicant's claims do not require that pH

differential is the means by which delivery is accomplished and, thus, pH is not implicit in the claims.

Examiner has duly considered Applicant's arguments but deems them unpersuasive.

As indicated above, in Hardy et al., the polymer and the pH range in which it dissolves is critical to the prevention of release of a drug until the composition reaches the terminal ileum or colon; too high a pH and the invention fails to work as no therapeutically effective amounts of the drug are absorbed, too low a pH and the drug is release before the composition reaches the terminal ileum or colon. Although claim 57 includes an effective amount of a drug, the claim does not appear to require that the drug be effective to treat the diseases listed in the preamble.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 29, 32-36,38-41,48-57 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over GB 1017674.

GB 1017674 expressly discloses a coated pharmaceutical composition, in the form of a granulate, tablet or gelatin capsule, which prevents release of alkali metal salicylate until the

colon falling within the scope of applicant's claims (Column 1, lines 9-20, Column 6, lines 83-125, Claims 4, 8).

Alternatively, at the very least the claimed invention is rendered obvious within the meaning of 35 USC 103, because the prior art discloses products and uses that contain the same exact ingredients/components as that of the claimed invention. See In re Fitzgerald, 205 USPQ 594 (CCPA 1980). See also In re May, 197 USPQ 601, 607 (CCPA 1978).

Conclusion

Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 3/17/2003 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609(B)(2)(i). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier number for accessing the facsimile machine is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Choi whose telephone number is (703) 308-0067. Examiner maintains a flexible schedule. However, Examiner may generally be reached Monday-Friday, 8:00 am – 5:30 pm (EST), except the first Friday of the each biweek which is Examiner's normally scheduled day off.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Mr. Thurman Page, can be reached on (703) 308-2927. Additionally, Technology Center 1600's Receptionist and Customer Service can be reached at (703) 308-1235 and (703) 308-0198, respectively.

FIC
October 20, 2003

S. MARK CLARDY
PATENT EXAMINER
GROUP 1600